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The Causes of Epidemics and the Laws which regulate their course

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SECTION XVIII

HYGIENE AND PREVENTIVE MEDICINE

INDEPENDENT PAPER

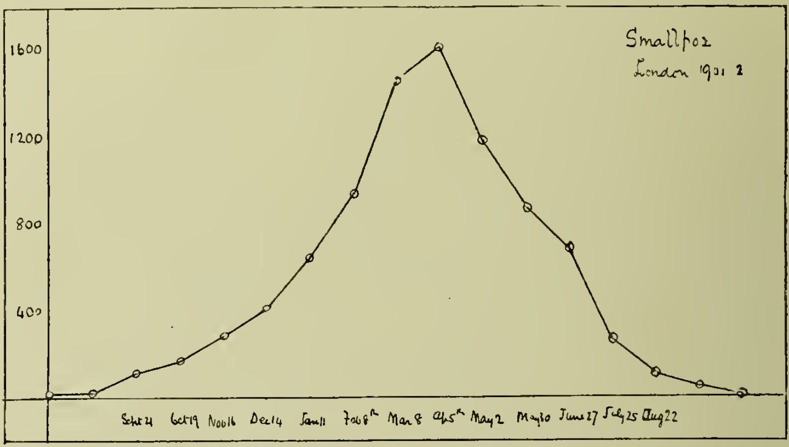
THE CAUSES OF EPIDEMICS AND THE LAWS WHICH REGULATE THEIR COURSE

By JOHN BROWNLEE, M.D., D.Sc.

The investigation of the different causes which determine the course of epidemics is at present very incomplete. A proper mathematical form for the progress of an epidemic is not yet known, and though approximations adequate to describe a solitary epidemic may be obtained, these are not sufficiently accurate to admit of application for the purposes of prediction.

Some points are, however, quite obvious. A very cursory examination of the data at our disposal shows that though modern hygiene may to some extent have limited the size of epidemics, it has done almost nothing to alter their form. Thus the great epidemic of small-pox in London in 1902 ran a course precisely similar to that seen in like epidemics in the eighteenth century, both in its rise and fall. In this case and in all infectious diseases the epidemic form is essentially the same. The rise and fall are roughly symmetrical (Diagram). But this form is not confined to the infectious diseases ; a more or less like law applies to any form of life, and can be easily observed if some organism which multiplies itself sufficiently quickly is chosen. To take an example ; the number of flies increases rapidly during the summer months and the curve of the number of flies present each day during the summer, essentially represents the same form as that of an epidemic. As an introduction to the subject this example may perhaps be discussed more fully.

It is not commonly thought, and in fact, even after special explanation, not easily believed by many people, that an epidemic is on the decline from the moment it begins. If, however, the number of flies caught per week is considered, it is readily seen that the ratios of the numbers from week to week are declining ratios. Thus taking the year 1908 the number of flies caught in London in the last week of June was 2,700, a fortnight later it was 5,500, a fortnight later 8,900, after another fortnight 13,500, and then the decline began. Thus, though the ascent is continuous, the ratio of increase is consecutively smaller in spite of the weather being favourable for the propagation of the fly. With each generation the energy of fertility present at the beginning definitely declines, or, to state it differently, the number of flies does not increase in a geometrical ratio, as might be assumed. The powers of reproduction continuously decrease. It is this fact which gives the typical form to all epidemics, and unless this fact is realized no satisfactory basis for a theory of epidemic can be devised. I have held this view for many years, and I find it is the same as that arrived at by Professor Minot as regards life in general. He holds that from the moment the cell is fertilized the organism is progressively dying till death, and that the rate of dying is quickest in the earliest years. Thus in man the percentage growth in the first month after birth is 23, in the second 17, &c., till between the eleventh and twelfth month it is only 2·8. This general theory would then seem to apply very widely. It suggests naturally that the principles of physical chemistry may be applied to the rate of growth, and that increase in size or in number depends on the presence of some substance which decays according to the rates shown in physical chemistry reactions. The life processes must of course be much more complex, but I personally see no reason why they should differ fundamentally. That some such relationship existed was first noted by Farr in 1866, and he stated it in the form that the second differences of the logarithms of the ordinates of the epidemic wave were constant. In modern language this means that the normal curve of chance would describe the epidemic. It also means that the rate of energy of increase in the organism declines according to the law of the mono-molecular reaction in physical chemistry, i.e. in a geometrical progression. It is to be noted that this also holds clearly for the figures given by Minot[1] for the rate



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[1] Minot, *The Problem of Age, Growth, and Death*, p. 117.

of increase in weight in children in the first twelve months, as is seen in annexed Table.

TABLE

Showing Rates of Growth of Children from 0–12 Months

Age in Months.	*Rate of Increase.*		*Age in Months.*	*Rate of Increase.*	
	Actual.	*Theoretical.*		*Actual.*	*Theoretical.*
0–1	23	20.6	6–7	6·4	6·5
1–2	17·5	16·9	7–8	5·3	5·3
2–3	14·0	14·0	8–9	4·4	4·4
3–4	11·0	11·4	9–10	3·6	3·6
4–5	9·2	9·5	10–11	3·0	3·0
5–6	7·7	7·8	11–12	2·8	2·5

The chief difference is seen at the ages 0–2 months. Such a law can hardly be expected to hold for our whole life when so many different factors in growth, such as development at puberty, &c., come in. Nor can it be expected to hold for a whole epidemic, but in many cases it gives a first approximation. How it applies may perhaps be seen by a simple example. Let the infectivity at the beginning be represented by 8 and the loss of infectivity at each period of time be ½, then if one person were originally infected we would have the numbers infected at each period of the epidemic given by the terms

$$1,\ 1\times 8,\ 1\times 8\times(8\times\tfrac{1}{2}),\ 1\times 8\times(8\times\tfrac{1}{2})\times(8\times\tfrac{1}{4}),$$
$$1\times 8\times(8\times\tfrac{1}{2})\times(8\times\tfrac{1}{4})\times(8\times\tfrac{1}{8}),\ \&c.,$$

or

$$1,\ 8,\ 32,\ 64,\ 64,\ 32,\ 8,\ 1.$$

So that the epidemic is symmetrical.

If the population susceptible to the disease were becoming exhausted the decline would be quicker than the rise. As a matter of fact it is generally slower, so that the infectivity is not lost quite at the rate of a geometrical progression, but rather more slowly. That an epidemic ceases from lack of susceptible persons will rarely be found probable if a census of the persons who have not suffered from the disease is taken at the close of the epidemic.

For instance, after the great epidemic of measles in Glasgow in 1907 and 1908, a careful note was taken of the previous infectious diseases experienced by children who were admitted suffering from whooping-cough, and of 263 cases aged between eighteen months and nine years, 126, or nearly half, had not passed through the attack of measles.

With regard to the variability of the infectivity of organisms at different times there is a certain amount of direct evidence. Some years ago I gave a table showing the liability of wards to cross-infection when persons incubating measles were admitted to these wards. The figures in this table demonstrated that when the number of admissions of cases of measles were few, i. e. in inter-epidemic times, the liability to cross-infection was very small, but that when an epidemic was in progress hardly a ward escaped cross-infection if a child incubating the disease were admitted to the ward. My observations in this matter since then have shown an even more marked difference than when the previous record was made. From January to August 1909 there was almost no measles in Glasgow. In this period four children were admitted incubating the disease, and in no case did cross-infection of the ward occur. In September a very large epidemic began which lasted till January. On ten occasions children incubating the disease were admitted, and in every case secondary cases occurred in the ward. After this, till April 1911, no child was admitted incubating the disease, when a long chronic epidemic began which lasted till May 1912. Between these dates nine children were admitted incubating the disease; cross-infection occurred in seven instances and no cross-infection in two. From July 1912 till March 1913 there was again a great dearth of measles in Glasgow, and in this period opportunity of cross-infection due to the presence of persons in the incubating stage was afforded six times without result. In one of these cases the patient was a nurse who, thinking she had a cold, remained on night duty for three nights in a ward which contained forty patients, and yet no secondary case developed. Since April of this year we have had again a small epidemic, and in three instances wards have become cross-infected.

Exactly the same kind of phenomenon is seen in small-pox. At the present moment this disease seems to have little infectivity. A patient suffering from it, having been infected abroad, recently developed an attack in Glasgow, and though he went about till the eruption was well out, attending places of public resort, such as music-halls, and travelling in trains, no secondary case of infection occurred. How the increase of infectivity which determines an epidemic takes place is at present quite unknown, but that it does take place there is, I think, no doubt. Some process whereby reproductive energy is stored up seems to exist not only in micro-organisms but in larger forms of life, and plagues of different animals are perfectly well known to occur without any direct antecedents that can be charged with their causation. These are perhaps more often observed among rodents, a recent plague of voles in the south of Scotland being a notable instance. Even after all the evidence regarding such plagues had been collated the Government commissioners were quite unable to offer any explanation why such plagues should occur.

In the preceding remarks I have not discussed the point as to whether varying susceptibility on the part of the attacked persons may not be the cause of the rise and the decline of epidemics. Though I cannot give all the evidence in this place I am satisfied that such an explanation can only hold in a few instances. A large number of diseases give rise to epidemics at different seasons of the year which run almost identical courses independently of the season. Thus the epidemics of influenza in London in 1891 and in 1891–92 are almost identical in form, though the maximum of the first was in May and of the second in January. Now if the passing from spring to summer causes the decline of an epidemic in a definite manner, it can hardly be expected that the passage from winter to spring will cause a decline of an exactly similar nature.

It is thus to be premised that in all epidemics, whether communicated directly or mediately through mosquitoes, fleas, &c., a loss of reproductive energy takes place. There is even some little evidence to show that the greater this power is at the commencement of an epidemic the more rapidly it is lost.

The effect which climatic conditions produce now falls to be discussed. These may act either directly or indirectly; directly, by rendering more favourable the environment in which the organism grows; indirectly, by crowding persons together as in winter, so that infection is more easily communicated. The former is the more important, and there is one disease which possesses special advantages for the investigation of the effects produced, namely, ‘ zymotic enteritis ’ or the ‘ summer diarrhœa ’ of children. This disease comes regularly every year; it does not vary in cycles of years, as scarlet fever and enteric fever, and is therefore specially suitable for statistical treatment. The amount, the date at which the epidemic reaches its height, the temperatures and rainfalls of the months when the epidemic occurs, are data which are easily accessible. The size of a city like London is also sufficient to give figures sufficiently large to reduce the element of probable error. The total number of years' statistics which are readily available, though not great, is considerable. The data used in this paper are figures for the forty-nine years 1861–1909.

The only method by which association of climate and disease can be measured at the present time is that of correlation. It is not by any means completely satisfactory, because it is a method which can only be applied under certain conditions which are not fulfilled with regard to summer diarrhœa, but in the absence of a better method the figures may be taken as approximately representing the truth. By the method of correlation a number is calculated which lies between −1 and 1. A correlation of unity represents complete relationship, which means that if the one factor is known the other can be absolutely predicted. When two things increase together, the correlation is positive; when as one increases the other decreases, the correlation is negative. A degree of correlation of ·5 and upwards is very fairly high. ·5 is that which is found between parents and children. A correlation of ·25 represents the relationship between uncle and nephew. Unfortunately with a problem such as this, where we have only fifty years of statistics, the probable error of each correlation coefficient is very considerable. I have not appended these errors to each value, but give here a table of the probable error for that number of observations for each value of the correlation from ·1 to 1 As no conclusion can be drawn unless the value of the correlation coefficient is more than three times its probable error, any correlation under ·2 is seen to be of very doubtful value.

Value of r.	*Probable error.*	*Value of r.*	*Probable error.*
·1	·095	·6	·061
·2	·092	·7	·049
·3	·088	·8	·034
·4	·081	·9	·018
·5	·072		

Correlation coefficients are of two kinds, the first expressing the direct relationship found from the figures, the other the relationship found when some second factor not considered in the first instance is assumed to be constant. The latter are called ‘partial’ coefficients. It is therefore necessary first to consider what are the relationships between the temperature and rainfalls of different months before inquiring into the relationships of the latter to the amount of diarrhœa. Between the temperatures of succeeding months the correlation is considerable, but between the temperature of months not consecutive it is nil. Thus the correlations between the temperatures in June and July, July and August, August and September, are respectively ·31, ·36, and ·38; while that between the temperatures of June and August is ·01, that between the temperatures of June and September—·03, and the like figures for July and September ·10. Further, when the correlation between the temperatures of June in two succeeding years is calculated, it is found to be ·05, and likewise that between the temperatures of July in succeeding years to be ·02. Thus in investigating the effect of temperature on diarrhœa we do not need to take into consideration any factor outside the months actually considered, namely, June, July, August, and September. When the rainfall is examined similar results are found. The effect of the rainfall on the temperature is important. Here the correlation is negative. The greater the rainfall the lower is the temperature. For June the value of the correlation is −·28, for July −·40.

With this introduction the following remarks may be made. There are two obvious points with reference to an epidemic of summer diarrhœa. First, the epidemic begins after the weather has been sufficiently warm, and second, the number of cases rapidly increases from almost zero to a maximum, and often declines as quickly, though the rate of fall is generally somewhat slower than that of the rise. There is no doubt at all about the influence of the temperature on the amount of the disease. In addition, however, there is evidently a distinct force tending to terminate the epidemic, even although the temperature remains high. The years 1895 and 1899 give very good illustrations of this. In the first of these the temperature remained at a high level for fully seven weeks after the crest of the epidemic was past, and though a certain amount of diarrhœa persisted, the wave of the epidemic was much lower. In the second case the crest of the wave was past and the fall begun long before the temperature showed any signs of falling. The factor previously stated, namely, that the organism loses its power of infecting or its power of propagation in some way from the onset of the epidemic onwards, thus also holds for summer diarrhœa. But temperature modifications of the epidemic are very definitely in evidence. A cold fortnight in the middle of an epidemic may cause it to temporarily decline, to rise again as the weather becomes warmer. Of these the years 1892 and 1900 furnish examples.

The special results of the application of the method of correlation gave, however, somewhat more accurate information, inasmuch that the relative influences of temperature and rainfall can be to some extent compared. To the total amount of diarrhœa present in an epidemic the temperatures of June, July, August, and September are correlated respectively as ·28, ·62, ·58, and ·43. Thus it is seen that the temperature of July has more to do with the amount of diarrhœa than that of any other month, and that a warm September will prolong an epidemic to a greater extent than a warm June will determine one. If, however, we consider the date of the maximum height of the epidemic, the temperature of June becomes of much greater importance. A warm June is associated with an earlier maximum and a cold June with a later, while though the temperature of July, as just seen, has much to do with determining the total amount of diarrhœa, and though the date of the maximum is never before the 29th or 30th week of the year, it has much less to do with the date of the maximum, the value of correlation between the temperature of June and the week of summer diarrhœa being −·40 and the like value for July −·23. This is especially interesting in view of the fact that the correlation between the amount of diarrhœa and the week of the maximum is practically zero, being equal to ·01. In interpreting the above figures, however, the correlation between the temperatures of the successive months already referred to should be considered, and to do this it would be more proper to proceed to discuss the partial correlation coefficients; but it is not necessary to give these details, since, though the actual coefficients are somewhat altered by this more elaborate method, the relative proportions are well maintained; and as the correlation figures are at best only approximate, and the difference between the two sets little more than the probable error, the further application seems unnecessary. With regard to the rainfall, however, some special remarks must be made. We find that the correlation between the rainfall in June and the amount of diarrhœa is −·26, that is to say, that with a wet June there is less diarrhœa, but the correlation between the rainfall and temperature is so high that when this is allowed for and the partial correlation between the amount of diarrhœa and the rainfall determined on the assumption that the temperature is constant, the correlation between the rainfall and the diarrhœa becomes zero. Quite otherwise is it when the week of the epidemic and the rainfall are considered. Here it is found that a wet June delays the maximum of the epidemic very markedly. The correlation in this case is ·44, and even when the correction is made for temperature it remains as high as ·38, so that a wet June by itself, apart from other influences, delays the maximum of the epidemic, but does not at all affect the total amount.

The facts just detailed throw, I think, a good deal of light on the nature of this epidemic. It would seem that there is a resting stage in the life-history of the organism, and that this resting stage passes, under climatic influences, into an active stage. This brings the epidemic, in a way, into line with ordinary plant life. A warm spring will determine early generation, but the amount of growth depends upon the continual warmth through the summer. In spite, however, of the length of the summer, this growth does not go on indefinitely. The annual cycle may be shorter or longer, but its total length cannot be prolonged beyond a certain amount. Where this resting stage is passed is not clear. It would seem most probable that it takes place somewhere in the soil, especially if that is polluted, and that it is spread from thence by some other means.

Certain other factors, however, have a great influence on the nature of the epidemic. It is found that moderately high correlations exist between certain aspects of succeeding epidemics. Thus, the correlation between the date of the maximum of the epidemic in succeeding years is ·42, that is to say, that a late epidemic in one year is associated with a late epidemic in the next year and vice versa. This might be explained on the grounds, either that late ripening ‘ seed ’ tends to germinate late, or that those ‘ seeds ’ which tend to germinate late, having come under the selective influence of the climate of the year, constitute the majority of the crop, and thus a late epidemic is determined in the succeeding year. That this influence is independent of the temperature and rainfall of the latter year is mentioned before, the correlation between the temperatures and the rainfalls in corresponding months of succeeding years being practically negligible. The total amounts of epidemics in succeeding years are also correlated positively, a large epidemic one year tending to be followed by a similar epidemic in the next. In this instance the correlation is less than in the previous, amounting to ·34.

These facts tend to show that an epidemic of summer diarrhœa is an organic phenomenon subject to laws of its own regarding its beginning and end, having relationships to a large number of factors, but open to great modifications on account of climatic associations. Before June begins the amount of the epidemic and its date are to a certain extent fixed. In June these are modified very largely according to the variations which take place in temperature and rainfall. The temperatures of July, August, and September finally determine the total amount of the epidemic.

Conclusions

1. That an epidemic is an organic phenomenon which is caused by the organism becoming suddenly infective and thereafter losing its infectivity at a rate approximating to a geometrical progression.

2. That the progress of an epidemic may be due to the above process acting either directly or indirectly ; directly, as in an epidemic of small-

pox, where the infection passes from one person to another ; indirectly, as in an epidemic of malaria, where the number of mosquitoes rises and falls according to approximately the same law.

3. That it is probable that the epidemic ends because of loss of infectivity on the part of the infected organism rather than because of a change in susceptibility of individuals towards the organism, as epidemics of the same disease often run identical courses whether occurring in winter or in summer.

4. With regard to summer diarrhœa it is evident that the type of epidemic is to a certain degree fixed before the onset, and that it is only secondarily modified by the climate.

5. That the date of the epidemic is determined (*a*) by the date of the epidemic in the previous year, (*b*) by the temperature in the month of June, and (*c*) by the amount of rainfall in the month of June.

6. That the amount of the epidemic is determined chiefly by the temperature in the month of July.